REMARKS

Status of the Claims

Claims 1, 3 to 5, 7 to 13, 18, 22 to 24, 26 to 31, and 34 were acted upon by the Examiner in the Office Action dated November 15, 2005. Claims 3 to 5, 7 to 13, 18, 22 to 24, 26, 27, and 34 have been amended. Claims 1 and 28 to 33 have been canceled. Claims 35 to 38 have been added. Accordingly, claims 3 to 5, 7 to 13, 18, 22 to 24, 26, 27, and 34 to 38 are presented for examination.

Summary of the Examiner's Action

Claim Rejections

Claims 7 to 13, 22 to 24, 26, and 34 stand rejected under 35 U.S.C. §103(a), as being unpatentable over Crespo (WO 97/33975, wherein the English version is US 6,248,588) in view of Engler (US 2003/0211598).

Claims 3 to 5, 7 to 13, 18, 22 to 24, 26 and 27 stand rejected under 35 U.S.C. §103(a), as being unpatentable over Crespo taken with Engler and further in view of Rolland (US 6,040,295) or Sene (WO 98/02522, wherein its English version is US 6,451,256).

Claims 3 to 5, 7 to 13, 18, 22 to 24, 26, 27, and 34 stand rejected under 35 U.S.C. §112, second paragraph.

Applicants respectfully traverse the Examiner's rejection.

Discussion

Amendments to the Claims

Applicants have amended claims 3 to 5, 7 to 13, 18, and 22 to 24 to depend, directly or indirectly, from claim 34. Accordingly, claims 3 to 5, 7 to 13, 18, and 22 to 24 have been amended to be directed to a "method" instead of a "composition".

Claims 26 and 27 have been amended for editorial purposes.

Claim 34 has been rewritten as an independent claim and has been amended to recite "a method of enhancing the titer of...". Support for the recitation "enhance the titer" is found on page 6, line 4 of the application. Support for the recitation "wherein the concentration of HSA is from about 0.01% to about 25% (w/v)" is found in originally filed claim 2. Support for the

recitation "stored at a temperature greater than about 4°C for at least about 3 months" is found Example 6 (page 33, line 29 to page 36, line 13) and Figure 11 of the application.

Support for new claims 35 to 38 is found on page 26, table 4, in formulation ID Nos. 13 and 14.

The 35 U.S.C. §103(a) Rejections

Claims 7 to 13, 22 to 24, 26, and 34 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Crespo in view of Engler et al. (US 2003/0211598). Applicants respectfully traverse the rejection.

With regard to a *prima facie* obviousness rejection, MPEP §2143 states:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.
>
> The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in Applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Accordingly, a proper *prima facie* case of obviousness requires that the combination teach all of the claim limitations. Applicants submit that the present rejection has not satisfied this requirement.

Presently amended claim 34, from which claims 7 to 13, 22 to 24, and 26 all depend directly or indirectly, is directed to:

A method of enhancing the titer of or preserving recombinant adenovirus vectors or particles comprising:

a) preparing a purified sample of said recombinant adenovirus vectors or particles;

b) mixing said sample with a composition comprising human serum albumin (HSA), wherein the concentration of HSA is from about 0.01% to about 25% (w/v), wherein the pH of said composition is greater than or equal to 5.0 and less than or equal to 9.0; and

c) storing said recombinant adenovirus vectors or particles at a temperature greater than about 4°C for at least 3 months.

Applicants submit that neither Crespo nor Engler et al. disclose the step of "storing said recombinant adenovirus vectors or particles at a temperature greater than about 4°C for at least 3 months".

Column 10, lines 26 to 30, of Crespo recites:

> A medium according to the invention allows the freezing and thawing of biological material under conditions of high viability. The media according to the invention may, in particular, allow the freezing of biological material at temperatures of between -200 and -4 degrees Celsius.

Accordingly, Crespo discloses a solution for freezing adenovirus. Indeed, on page 3 of the present action the Examiner states that Crespo "does not specifically recite that the medium is effective to stabilize the virus at temperatures greater than about 4°C ".

Despite this acknowledgment that Crespo does not specifically disclose storage of adenovirus at temperatures within the claimed range, the Examiner further asserts that Crespo teaches that biological material stored in the medium of Crespo has high viability upon thawing and that "temperatures of about 4°C to about 20°C represent conditions of thawing".

Applicants submit that, according to Crespo, temperatures of about 37°C, not temperatures greater than about 4°C, represent conditions of thawing. Column 13, lines 25 to 27, of Crespo recites:

> The ampoule to be thawed is dipped into the pot of sterile water at about 37 degrees Celsius, without submerging it, with gentle stirring until the ice completely disappears.

Accordingly, Applicants submit that Crespo does not teach the recitation of "storing said recombinant adenovirus vectors or particles at a temperature greater than about 4°C".

In addition, the Examiner has not addressed the recitation of "storing...for at least 3 months" in claim 34. Applicants submit that even if Crespo did disclose storage at temperatures greater than about 4°C upon thawing, such storage would only be transient. Crespo does not disclose storage in the claimed temperature range for at least 3 months. Advantages for storing in this range include increased ease of manipulation of the adenovirus and decreased loss of viability due to the freeze-thaw cycle.

For the reasons noted above, Crespo does not disclose compositions useful for preserving adenovirus at temperatures in the claimed range for the claimed time period and there is no evidence to suggest that the compositions of Crespo would be effective at these temperatures. In contrast, the presently claimed invention is effective at temperatures greater than about 4°C. Engler et al., which relates to delivery-enhancing agents and has been cited for the teaching of a Tris-HCl buffer, provides no basis to overcome the deficiencies of Crespo. Accordingly, the Examiner has not satisfied the requirement of teaching or suggesting all the claim limitations.

If the Examiner still believes that a *prima facie* case of obviousness has been demonstrated, Applicants submit that the present invention is nonobvious in view of the objective evidence presented below.

MPEP §2141 states (emphasis added):

> Objective evidence or secondary considerations such as unexpected results, commercial success, long-felt need, failure of others, copying by others, licensing, and skepticism of experts are relevant to the issue of obviousness and must be considered in every case in which they are present. When evidence of any of these secondary considerations is submitted, the examiner must evaluate the evidence.

Accordingly, MPEP §2141 requires that objective evidence such as unexpected results be considered when evaluating whether an invention is obvious. In the present application, Figure 11 on page 43 of the application provides such evidence. Figure 11 depicts results wherein the presently claimed composition maintains the titer of adenoviral particles for over about 3 months at 4°C and 20°C. Such results would not be expected by one of skill in the art upon reviewing Crespo (directed to freezing solutions) and Engler et al. (directed to delivery-enhancing agents). Indeed, there are no disclosures in the prior art, including Crespo and Engler et al., that are predictive of this dramatic and unexpected viral stability at these increase temperatures.

Accordingly, applicants respectfully request that the rejection of claims 7 to 13, 22 to 24, 26, and 34 under 35 U.S.C. §103(a) as being unpatentable over Crespo in view of Engler et al. be withdrawn.

Claims 3 to 5, 7 to 13, 18, 22 to 24, 26 and 27 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Crespo taken with Engler et al. and further in view of Rolland et al. (US 6,040,295) and Sene (WO 98/02522, wherein the English version is US 6,451,256).

Applicants respectfully traverse the rejection.

Rolland et al. discloses compositions and methods for enhancing the uptake of nucleic acids by cells or organisms and has been cited for its teaching of an isotonic solution comprising 150 mM NaCl. Sene discloses methods for preserving viral particles in a sucrose solution and has been cited for its teaching of Tris-HCl buffer with pH between 8 and 9.

For the reasons noted above, the combination of Crespo and Engler et al. is non-obvious. Rolland et al. and Sene provide no basis to overcome these deficiencies. In addition, claims 3 to 5, 7 to 13, 18, 22 to 24, 26 and 27 have all been amended to depend directly or indirectly from claim 34. As claim 34 has not been found unpatentable over Crespo taken with Engler et al. and further in view of Rolland et al. and Sene, the present rejection of claims 3 to 5, 7 to 13, 18, 22 to 24, 26 and 27 cannot stand.

Accordingly, respectfully request that the rejection of claims 3 to 5, 7 to 13, 18, 22 to 24, 26 and 27 under 35 U.S.C. §103(a) as being unpatentable over Crespo taken with Engler et al. and further in view of Rolland et al. and Sene be withdrawn.

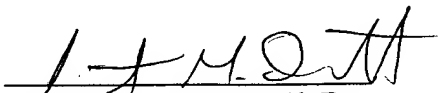
The 35 U.S.C. §112, second paragraph, Rejections

Claims 3 to 5, 7 to 13, 18, 22 to 24, 26, 27, and 34 stand rejected under 35 U.S.C. §112, second paragraph, for failing to particularly point out and distinctly claim the invention. In particular, the Examiner asserts that the concentration of HSA is unclear. Claim 34, from which claims 3 to 5, 7 to 13, 18, 22 to 24, 26, and 27 all depend directly or indirectly, has been amended to recite "wherein the concentration of HSA is from about 0.01% to about 25% (w/v)". Support for the recitation "wherein the concentration of HSA is from about 0.01% to about 25% (w/v)" is found in originally filed claim 2.

Accordingly, respectfully request that the rejection of claims 3 to 5, 7 to 13, 18, 22 to 24, 26, 27, and 34 under 35 U.S.C. §112, second paragraph, be withdrawn.

A favorable action on the merits is requested respectfully.

Respectfully submitted,



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